

Descriptive Epidemiology of Bipolar I Disorder Among United States Military Personnel

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ABSTRACT Psychiatric disorders in military members require substantial medical, administrative, and financial resources, and are among the leading causes of hospitalization and early discharge. We reviewed available data to better understand the incidence of bipolar I disorder among military personnel. Defense Medical Epidemiology Database inpatient data were used. Descriptive and comparative statistics were performed. From 1997-2006 there were 3,317 first hospitalizations for bipolar I disorder with a mean of 1.2 hospitalizations per case. The rate of first occurrence among this adult population was 0.24 per 1,000 person-years. The incidence increased over time for depressed and mixed episode types among both genders. High risk groups include women, younger individuals, and whites. This population provides insight into adult onset bipolar I disorder incidence and demographic patterns not available elsewhere and offers potential opportunities to improve its understanding.

INTRODUCTION

Bipolar disorder is one of the most debilitating disorders in the developed world according to the World Health Organization (WHO).¹ According to the Diagnostic and Statistical Manual of Mental Disorders the essential feature of bipolar I disorder is a clinical course that is characterized by the occurrence of one or more manic or mixed episodes. Often individuals have also had one or more major depressive episodes.² The lifetime prevalence of bipolar I disorder in the United States is approximately 1.0% (range 0.7-1.6%)³⁻⁶ and twelve month prevalence is about 0.6%,³ but the numbers are inconsistent across different sources.^{4,7,8} There is a lack of bipolar I disorder incidence data and temporal trends, specifically for diagnostic and demographic subgroups. While some results suggest a modest increase in the rates of mania and bipolar I disorder over the last decades, the examination of temporal trends have various methodological limitations, should be interpreted with caution, and warrant further research.^{4,9,10}

While the majority of previous research established that bipolar disorder is unrelated to gender,^{1,3,11} some^{7,12-14} but not other^{15,16} studies reported that women are more likely to present with an initial depressive episode,¹⁴ exhibit more depressive and less manic symptoms,^{17,18} and have a higher number of depressive episodes in the course of bipolar affective dis-

order¹² compared with men. Whereas men have a higher number of manic episodes at the onset¹⁹ and during the entire course of bipolar disorder,¹² as well as earlier onset of manic episodes⁷ and bipolar disorder.^{13,14}

There are very few consistent findings in existing literature on race and ethnic differences for bipolar I disorder incidence.^{10,11,20-24} The discrepancies could be at least partially attributed to the dissimilarity of the captured populations (e.g., outpatient vs. inpatient, the United Kingdom vs. United States etc.) as well as to a differential diagnostic bias reported in a few studies.^{25,26}

While the reported mean age of bipolar I disorder onset among US population is 18.1-18.2 years,^{1,3} some studies argue that there are a few different age-at-onset subgroups of bipolar patients with various underlying familial vulnerability factors.²⁷⁻²⁹

As an important source of medical and occupational morbidity among active-duty US military personnel, psychiatric disorders in general^{30,31} and affective disorders in particular represent significant occupational burden, disrupt unit cohesion and readiness, and disproportionately consume medical and administrative resources.

In the US military psychiatric illness is the second leading cause of hospitalizations (Incidence Rate (IR) = 7.14 per 1,000 PY) after injury and poisoning for men, and (IR=12.48 per 1,000 PY) after delivery-related hospitalizations for women.³² In addition to being a primary cause of hospitalizations within 1 and 2 years of accession,³³ mental disorders as a primary hospital discharge diagnosis lead to a high attrition rate (45%) within 6 months for those hospitalized for the first time.³⁴ The affective disorder (ICD-9: 296) is the third most common reason for overall hospitalizations, the second most frequent cause for mental disorder hospitalizations, and the fourth most prevalent diagnosis among mental disorder ambulatory visits³² in the military.

The purpose of this study is to describe the epidemiology of bipolar I disorder among hospitalized military personnel.

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In particular we explored the time trends of incidence rates over the ten year period, examined incidence rates of adult onset bipolar I disorder manic, depressed, mixed, and NOS (not otherwise specified), and compared incidence rates by gender, race, and age groups.

METHODS

We used the Defense Medical Epidemiology Database (DMED) application that provides a remote access to a subset of data contained within the Defense Medical Surveillance System (DMSS). Operated by the Armed Forces Health Surveillance Center, DMSS contains current and chronological data on diseases and medical events (ICD-9 codes) such as hospitalizations, ambulatory visits, and reportable diseases. It also provides longitudinal data pertinent to personnel characteristics and deployments experienced by all active duty and reserve component service members. We reported incidence rates based on the hospitalizations for the years 1997-2006. The first occurrence was used to report incidence.

Those hospitalized with the primary diagnosis of (ICD-9 codes) 296.4 (Bipolar Affective Disorder, Manic), 296.5 (Bipolar Affective Disorder, Depressed), 296.6 (Bipolar Affective Disorder, Mixed), and 296.7 (Bipolar Affective Disorder, NOS) were defined as cases with bipolar I disorders. All the above mentioned ICD-9 diagnostic codes are compatible with the DSM-IV and share the same code numbers. Since ICD-9 codes 296.0 (Manic Disorder, Single Episode) and 296.1 (Manic Disorder, Recurrent Episode) have a very low incidence rates (<0.02 per 1,000 person-years) in the DMED data set and 296.1 is not present in the DSM-IV, these codes were not included in the bipolar I disorder case definition.

Incidence rates (IR), defined as counts of hospitalized persons divided by person-years at risk for the cohort members, multiplied by 1,000, have been obtained from the DMED. Incidence rate ratio (IRR) is calculated by dividing the rate of bipolar I disorder in one demographic group by the rate in the other demographic group, with statistical significance determined by the 95% confidence interval (95%CI) around the point estimate.³⁵ The time trend in the incidence rates was evaluated by using Spearman's correlation coefficients (r_s).³⁶

The results are presented for different types of bipolar I disorder and stratified by sex, race, age groups, branch of service, and a year of hospitalization. Race is self-reported as white, black, and other, with comparisons made only between white and black. Age is grouped as younger than 20, 20 to 24, 25 to 29, 30 to 34, and ≥ 35 . Branch of service includes Army, Navy, Air Force and Marines.

RESULTS

A total of 2,512 men and 805 women were hospitalized for bipolar I disorder for the first time during the study period (13,512,425 person-years). The overall IR was 0.21 (95%CI: 0.20; 0.22) for men and 0.40 (95%CI: 0.38; 0.43) for women.

The average number of hospitalizations per person for affective disorder was 1.27, of which 1.16 was for the same diagnosis, and 1.11 for a different type of bipolar I disorder episode (4th digit 4 through 7 of ICD-9 code '296').

The overall IR was highest for bipolar disorder manic (IR=0.08), followed by NOS (IR=0.07), depressed (IR=0.05), and mixed (IR=0.04). Among men (Table I) and women (Table II) the rate of bipolar I disorder was higher among whites than blacks. Only manic type was not significantly more common among whites, with an IRR of 0.82 (0.70, 0.96) among men and 1.10 (0.81, 1.51) among women. The IRR for white versus black service members ranged from 0.82 to 2.69 among men and from 1.10 to 2.64 among women for manic and depressed episodes respectively.

Among both whites and blacks the overall rates of bipolar I disorders were higher in women than men (Table III). Except for manic type among blacks, all types were signifi-

TABLE I. Bipolar I Incidence Rates (per 1,000 person-years) and Rate Ratios by Race (White vs. Black) among Men

	White		Black		Rate Ratio	95% CI	
	Count ^a	Rate	Count ^b	Rate		Lower	Higher
Manic	633	0.076	192	0.092	0.82	0.70	0.96
Depressed	369	0.044	34	0.016	2.69	1.89	3.82
Mixed	364	0.043	45	0.022	2.01	1.47	2.73
NOS	569	0.068	96	0.046	1.47	1.18	1.82
All episodes	1935	0.231	367	0.177	1.31	1.17	1.46

^a per 8,382,415 person-years at risk. ^b per 2,078,708 person-years at risk.

TABLE II. Bipolar I Incidence Rates (per 1,000 person-years) and Rate Ratios by Race (White vs. Black) among Women

	White		Black		Rate Ratio	95% CI	
	Count ^a	Rate	Count ^b	Rate		Lower	Higher
Manic	118	0.104	59	0.095	1.10	0.81	1.51
Depressed	134	0.119	28	0.045	2.64	1.75	3.96
Mixed	120	0.106	25	0.040	2.64	1.72	4.07
NOS	194	0.172	46	0.074	2.32	1.68	3.20
All episodes	566	0.501	158	0.254	1.97	1.65	2.35

^a per 1,129,516 person-years at risk. ^b per 622,067 person-years at risk.

TABLE III. Bipolar I Disorder Female to Male Incidence Rate Ratios by Race

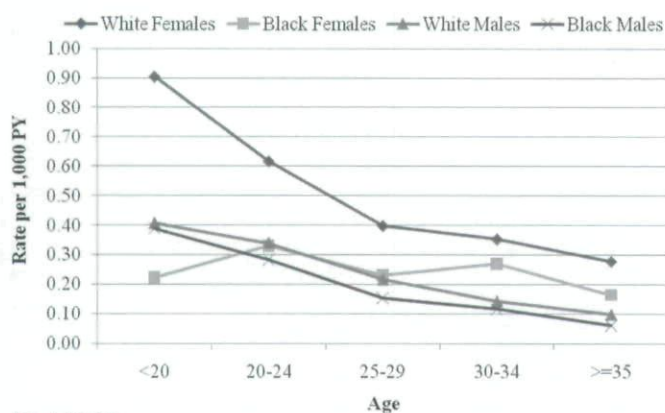
	White			Black		
	Rate Ratio	95% CI		Rate Ratio	95% CI	
Manic	1.38	1.14	1.68	1.03	0.77	1.37
Depressed	2.69	2.21	3.28	2.75	1.67	4.54
Mixed	2.45	1.99	3.01	1.86	1.14	3.03
NOS	2.53	2.15	2.98	1.60	1.13	2.28
All episodes	2.17	1.98	2.38	1.44	1.19	1.73

cantly higher in women than men. The lowest IRR for females to males was for manic and the highest was for depressed episode in both white and black groups.

Among men, black and white, and among white women, the IR significantly decreased with age. There was no significant IR change with age among black women (Fig. 1).

At all ages the IR was highest among white women. In the youngest age group the IR among black women was lowest of all, but by age group 25-29, the IR was exceeded only by white women.

We examined time trends for the overall incidence rate (results not shown), as well as the rates of different episodes of bipolar I disorder in men and women, as shown in Figures 2 and 3 respectively. Overall linear time trend for males ($p = 0.06$) and females ($p = 0.99$) were not significant. When the rates among men are observed before and after 2001, there was a significant increase from 1997 (IR=0.17) to 2001 (IR=0.27, $p = 0.03$) and the rates stabilized after that averaging 0.22/1,000 per year. For bipolar I episodes, among men there was a significant increase in the rates of bipolar I disorder mixed ($r_s = 0.927$, $p < 0.001$) and depressed ($r_s = 0.879$, $p < 0.001$), both starting at 0.02 in 1997 and reaching 0.06 in 2006. Among women the IR increased significantly ($r_s = 0.842$, $p < 0.001$) for mixed and borderline significantly ($r_s = 0.576$, $p = 0.05$) for depressed episodes from respectively 0.07 and



*Per 1,000PY

FIGURE 1. Incidence rates of bipolar I disorder by gender, race, and age*

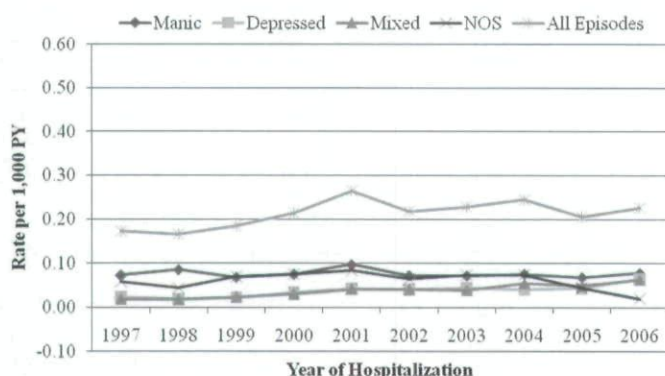
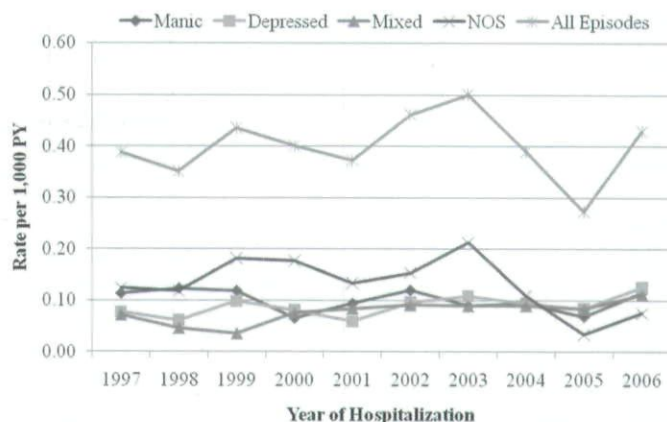


FIGURE 2. Incidence of bipolar I disorder by year among men.



* The incidence rates for women are less stable due to the smaller counts.

FIGURE 3. Incidence of bipolar I disorder by year among women.*

0.08 in 1997 to 0.11 and 0.13 in 2006. No significant change was found for bipolar manic or NOS in either gender.

Given that the first hospitalization could only be obtained for a single selection of an ICD-9 code, we were unable to directly compare the rate of bipolar I disorder with the entire category of affective (ICD-9 296) and psychiatric (ICD-9 290-319) disorders. When any inpatient encounter was taken into consideration the rate was 0.29 per 1,000 PY for bipolar I disorder, 1.50 for affective disorder, and 6.93 for all mental disorders combined. Thus hospitalizations for bipolar I disorder roughly represent about 20% of the affective and 4% of all psychiatric disorders hospitalizations.

DISCUSSION

We directly measured the incidence rate of hospitalizations for new adult-onset bipolar I disorder among military personnel. The incidence of hospital-diagnosed bipolar I disorder varied substantially by age, sex, and race. High risk groups include women, younger service members, and whites. Over time IR increased for bipolar disorder mixed and depressed among both genders, but the patterns are more clearly seen among men.

Some previous studies have reported that bipolar disorder is unrelated to gender.^{1,3,11} However, we found a significantly and substantially higher rate of bipolar I disorder among women compared with men. Our findings are consistent with Blader and Carlson's study where they examined hospital discharges from 1996 to 2004. The rate of bipolar disorder in adult white women was higher compared with their male counterparts for the entire study period and a much smaller difference was reported between adult black women and men only between 1996-2001.¹⁰

We found that the overall rate of bipolar I disorder was higher in whites compared with blacks which is consistent with Blader et al. and Averill et al.^{10,37} However, there are few consistent findings in existing literature on race and ethnic differences for bipolar I disorder incidence. Some sources report no race difference,²⁰⁻²² while others report higher rates of bipolar

disorder and mania in African Caribbeans and Africans living in the United Kingdom.^{11,23,24} Blader and Carlson report that more white women are diagnosed with bipolar disorder than black women from 1996 to 2002, and that black men had lower rates of bipolar disorder diagnoses from 1996 to 2000.¹⁰

Our finding that the highest female to male ratio was for bipolar disorder depressed is supported by some studies.^{14,18} The lowest female to male ratio found for bipolar disorder manic among whites, and no gender difference among blacks, may be at least partially explained by men's higher propensity toward manic episodes.^{12,19,22}

We found the highest occurrence of bipolar I disorder incidence in the age group below 20 years followed by those in their 20-24 and further decrease as a function of age among white men and women and black men. These findings are consistent with prior reports.^{1,3,20} The observed increase in the incidence of bipolar I depressed among men and mixed episode for both genders from 1997 to 2006 justifies closer attention and further studies of temporal trends in the entire US population.

Our study has a number of strengths. Because military applicants undergo thorough medical examination and medical history review before accession, it is unlikely that many overtly psychotic or clinically depressed persons enter the military. Although some persons may not reveal their medical history and enter during periods of remission, from 2001 to 2006 on average 54 (or 3% of all psychiatric discharges) service members were discharged per year with bipolar I disorder existing prior to service.³³ Thus the overwhelming majority of the cases included in the study are incident adult onset bipolar I disorder. Provided that the vast majority of the mental health hospitalizations of service members are to military treatment facilities,²⁹ the ascertainment rate of the incident cases is high. Since the length of time in service is available for every soldier, we used person-time at risk for the study period as the denominator to capture the incidence rate by person time at risk. The availability of demographic information on every service member allowed us to measure incidence density in demographically diverse subpopulations.

Several limitations of the current study merit attention. Given that the number of hospitalized with bipolar I disorder is calculated as a sum of hospitalizations with four different episode types based on the ICD-9 diagnostic code (manic, depressed, mixed, and NOS), individuals could be counted more than once if they were rehospitalized with a different episode type of bipolar I disorder. However, the incidence rates cannot be overestimated by more than 11% since the average number of hospitalizations for different types of bipolar I disorder episodes was 1.11 per person as estimated in the result section.

Cases are defined hospitalizations; therefore, as mentioned, cases that did not require hospitalization or were hospitalized outside of the Military system were not captured by this study, leading to an underestimation of the total incidence of bipolar

I disorder. Such an approach, however, allows more certainty in the diagnosis because of the more extensive observation and evaluation of hospitalized patients.

Incidence rates for women were less stable than for men due to the lower numbers of female cases and service members. No analyses can be conducted on an individual level with this data. The healthy worker effect due to preaccession medical examination as well as periodic personnel and medical evaluations while in the military may limit generalization to the entire US population of young adults.

Although the population studied is generally healthier than the US civilian population due to preaccession medical screening, easy and equal access to medical care, and comprehensive preventive medical programs, the military population includes individuals of both sexes, all racial, ethnic, and socioeconomic groups from all over the United States and many foreign countries. All outpatient and inpatient medical encounters financed by the government are captured, and the high degree of bipolar disorder ascertainment allows for calculation of rates overall and among demographic subgroups. Therefore, this study provides valuable insight into adult-onset bipolar disorder incidence and difference between sub-groups not available elsewhere.

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